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SEQUENCE LISTING

RECEIVED  
APR 28 2003  
TECH CENTER 1600/2900

<110> Ingham et al.

<120> SCREENING ASSAYS FOR HEDGEHOG AGONISTS AND ANTAGONISTS

<130> HMSU-P14-006

<140> 09/711724

<141> 2000-11-13

<150> 08/674509

<151> 1996-07-07

<160> 55

<170> PatentIn version 3.1

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Glu Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr  
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Glu Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys  
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Tyr Tyr Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn  
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Ser Val Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val  
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His Leu Glu His Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly  
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Asp Arg Val Leu Ala Ala Asp Ala Asp Gly Arg Leu Leu Tyr Ser Asp  
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Untitled

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Arg Val Tyr Val Leu Gly Glu Gly Gly Gln Gln Leu Leu Pro Ala Ser  
305 310 315 320

Val His Ser Val Ser Leu Arg Glu Glu Ala Ser Gly Ala Tyr Ala Pro  
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Ala His Arg Ala Phe Ala Pro Leu Arg Leu Leu His Ala Leu Gly Ala  
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Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Val His  
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Phe Pro Ala Gly Ala Gln Val Arg Leu Glu Asn Gly Glu Arg Val Ala



Untitled

130

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140

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Arg Leu Ala Leu Thr Pro Ala His Leu Leu Phe Ile Ala Asp Asn His  
195 200 205

Thr Glu Pro Ala Ala His Phe Arg Ala Thr Phe Ala Ser His Val Gln  
210 215 220

Pro Gly Gln Tyr Val Leu Val Ser Gly Val Pro Gly Leu Gln Pro Ala  
225 230 235 240

Arg Val Ala Ala Val Ser Thr His Val Ala Leu Gly Ser Tyr Ala Pro  
245 250 255

Leu Thr Arg His Gly Thr Leu Val Val Glu Asp Val Val Ala Ser Cys  
260 265 270

Phe Ala Ala Val Ala Asp His His Leu Ala Gln Leu Ala Phe Trp Pro  
275 280 285

Leu Arg Leu Phe Pro Ser Leu Ala Trp Gly Ser Trp Thr Pro Ser Glu  
290 295 300

Gly Val His Trp Tyr Pro Gln Met Leu Tyr Arg Leu Gly Arg Leu Leu  
305 310 315 320

Leu Glu Glu Ser Thr Phe His Pro Leu Gly Met Ser Gly Ala Gly Ser

Untitled

325

330

335

<210> 11  
 <211> 437  
 <212> PRT  
 <213> Mus musculus

<400> 11

Met Leu Leu Leu Leu Ala Arg Cys Phe Leu Val Ile Leu Ala Ser Ser  
 1 5 10 15

Leu Leu Val Cys Pro Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly  
 20 25 30

Lys Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe  
 35 40 45

Ile Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu  
 50 55 60

Gly Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn  
 65 70 75 80

Tyr Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp  
 85 90 95

Arg Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile  
 100 105 110

Ser Val Met Asn Gln Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly  
 115 120 125

Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly  
 130 135 140

Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly  
 145 150 155 160

# Untitled

Met Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr  
165 170 175

Glu Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val  
180 185 190

Ala Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu  
195 200 205

Glu Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Arg Pro Gly Asp Arg  
210 215 220

Val Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu  
225 230 235 240

Thr Phe Leu Asp Arg Asp Glu Gly Ala Lys Lys Val Phe Tyr Val Ile  
245 250 255

Glu Thr Leu Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu  
260 265 270

Leu Phe Val Ala Pro His Asn Asp Ser Gly Pro Thr Pro Gly Pro Ser  
275 280 285

Ala Leu Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val  
290 295 300

Ala Glu Arg Gly Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser  
305 310 315 320

Val Thr Leu Arg Glu Glu Glu Ala Gly Ala Tyr Ala Pro Leu Thr Ala  
325 330 335

His Gly Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val  
340 345 350

# Untitled

Ile Glu Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu  
355 360 365

Ala His Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Gly Gly  
370 375 380

Gly Gly Gly Ser Ile Pro Ala Ala Gln Ser Ala Thr Glu Ala Arg Gly  
385 390 395 400

Ala Glu Pro Thr Ala Gly Ile His Trp Tyr Ser Gln Leu Leu Tyr His  
405 410 415

Ile Gly Thr Trp Leu Leu Asp Ser Glu Thr Met His Pro Leu Gly Met  
420 425 430

Ala Val Lys Ser Ser  
435

<210> 12  
<211> 418  
<212> PRT  
<213> Danio rerio

<400> 12

Met Arg Leu Leu Thr Arg Val Leu Leu Val Ser Leu Leu Thr Leu Ser  
1 5 10 15

Leu Val Val Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Tyr Gly Arg  
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile  
35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly  
50 55 60

Lys Ile Thr Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr

Untitled

65

70

75

80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg  
85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser  
100 105 110

Val Met Asn His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp  
115 120 125

Asp Glu Asp Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg  
130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr  
145 150 155 160

Leu Ser Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu  
165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala  
180 185 190

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Leu Val Ser Leu Gln  
195 200 205

Asp Gly Gly Gln Lys Ala Val Lys Asp Leu Asn Pro Gly Asp Lys Val  
210 215 220

Leu Ala Ala Asp Ser Ala Gly Asn Leu Val Phe Ser Asp Phe Ile Met  
225 230 235 240

Phe Thr Asp Arg Asp Ser Thr Thr Arg Arg Val Phe Tyr Val Ile Glu  
245 250 255

Thr Gln Glu Pro Val Glu Lys Ile Thr Leu Thr Ala Ala His Leu Leu

Untitled  
265

260

270

Phe Val Leu Asp Asn Ser Thr Glu Asp Leu His Thr Met Thr Ala Ala  
275 280 285

Tyr Ala Ser Ser Val Arg Ala Gly Gln Lys Val Met Val Val Asp Asp  
290 295 300

Ser Gly Gln Leu Lys Ser Val Ile Val Gln Arg Ile Tyr Thr Glu Glu  
305 310 315 320

Gln Arg Gly Ser Phe Ala Pro Val Thr Ala His Gly Thr Ile Val Val  
325 330 335

Asp Arg Ile Leu Ala Ser Cys Tyr Ala Val Ile Glu Asp Gln Gly Leu  
340 345 350

Ala His Leu Ala Phe Ala Pro Ala Arg Leu Tyr Tyr Tyr Val Ser Ser  
355 360 365

Phe Leu Phe Pro Gln Asn Ser Ser Ser Arg Ser Asn Ala Thr Leu Gln  
370 375 380

Gln Glu Gly Val His Trp Tyr Ser Arg Leu Leu Tyr Gln Met Gly Thr  
385 390 395 400

Trp Leu Leu Asp Ser Asn Met Leu His Pro Leu Gly Met Ser Val Asn  
405 410 415

Ser Ser

<210> 13  
<211> 462  
<212> PRT  
<213> Homo sapiens  
  
<400> 13

# Untitled

Met Leu Leu Leu Ala Arg Cys Leu Leu Leu Val Leu Val Ser Ser Leu  
1 5 10 15

Leu Val Cys Ser Gly Leu Ala Cys Gly Pro Gly Arg Gly Phe Gly Lys  
20 25 30

Arg Arg His Pro Lys Lys Leu Thr Pro Leu Ala Tyr Lys Gln Phe Ile  
35 40 45

Pro Asn Val Ala Glu Lys Thr Leu Gly Ala Ser Gly Arg Tyr Glu Gly  
50 55 60

Lys Ile Ser Arg Asn Ser Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr  
65 70 75 80

Asn Pro Asp Ile Ile Phe Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg  
85 90 95

Leu Met Thr Gln Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser  
100 105 110

Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp  
115 120 125

Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg  
130 135 140

Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met  
145 150 155 160

Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu  
165 170 175

Ser Lys Ala His Ile His Cys Ser Val Lys Ala Glu Asn Ser Val Ala  
180 185 190

# Untitled

Ala Lys Ser Gly Gly Cys Phe Pro Gly Ser Ala Thr Val His Leu Glu  
195 200 205

Gln Gly Gly Thr Lys Leu Val Lys Asp Leu Ser Pro Gly Asp Arg Val  
210 215 220

Leu Ala Ala Asp Asp Gln Gly Arg Leu Leu Tyr Ser Asp Phe Leu Thr  
225 230 235 240

Phe Leu Asp Arg Asp Asp Gly Ala Lys Lys Val Phe Tyr Val Ile Glu  
245 250 255

Thr Arg Glu Pro Arg Glu Arg Leu Leu Leu Thr Ala Ala His Leu Leu  
260 265 270

Phe Val Ala Pro His Asn Asp Ser Ala Thr Gly Glu Pro Glu Ala Ser  
275 280 285

Ser Gly Ser Gly Pro Pro Ser Gly Gly Ala Leu Gly Pro Arg Ala Leu  
290 295 300

Phe Ala Ser Arg Val Arg Pro Gly Gln Arg Val Tyr Val Val Ala Glu  
305 310 315 320

Arg Asp Gly Asp Arg Arg Leu Leu Pro Ala Ala Val His Ser Val Thr  
325 330 335

Leu Ser Glu Glu Ala Ala Gly Ala Tyr Ala Pro Leu Thr Ala Gln Gly  
340 345 350

Thr Ile Leu Ile Asn Arg Val Leu Ala Ser Cys Tyr Ala Val Ile Glu  
355 360 365

Glu His Ser Trp Ala His Arg Ala Phe Ala Pro Phe Arg Leu Ala His  
370 375 380



# Untitled

Ala Leu Leu Ala Ala Leu Ala Pro Ala Arg Thr Asp Arg Gly Gly Asp  
385 390 395 400

Ser Gly Gly Gly Asp Arg Gly Gly Gly Gly Gly Arg Val Ala Leu Thr  
405 410 415

Ala Pro Gly Ala Ala Asp Ala Pro Gly Ala Gly Ala Thr Ala Gly Ile  
420 425 430

His Trp Tyr Ser Gln Leu Leu Tyr Gln Ile Gly Thr Trp Leu Leu Asp  
435 440 445

Ser Glu Ala Leu His Pro Leu Gly Met Ala Val Lys Ser Ser  
450 455 460

<210> 14  
<211> 312  
<212> PRT  
<213> Homo sapiens

<400> 14

Arg Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu Ala  
1 5 10 15

Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu  
20 25 30

Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu  
35 40 45

Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr  
50 55 60

Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr  
65 70 75 80

Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu His Ser

Untitled

85

90

95

Ala Ala Ala Lys Thr Gly Gly Cys Phe Pro Ala Gly Ala Gln Val Arg  
100 105 110

Leu Glu Ser Gly Ala Arg Val Ala Leu Ser Ala Val Arg Pro Gly Asp  
115 120 125

Arg Val Leu Ala Met Gly Glu Asp Gly Ser Pro Thr Phe Ser Asp Val  
130 135 140

Leu Ile Leu Leu Asp Arg Glu Pro His Arg Leu Arg Ala Phe Gln Val  
145 150 155 160

Ile Glu Thr Gln Asp Pro Pro Arg Arg Leu Ala Leu Thr Pro Ala His  
165 170 175

Leu Leu Phe Thr Ala Asp Asn His Thr Glu Pro Ala Ala Arg Phe Arg  
180 185 190

Ala Thr Phe Ala Ser His Val Gln Pro Gly Gln Tyr Val Leu Val Ala  
195 200 205

Gly Ala Pro Gly Leu Gln Pro Ala Arg Val Ala Ala Val Ser Thr His  
210 215 220

Val Ala Leu Gly Ala Tyr Ala Pro Leu Thr Lys His Gly Thr Leu Val  
225 230 235 240

Val Glu Asp Val Val Ala Ser Cys Phe Ala Ala Val Ala Asp His His  
245 250 255

Leu Ala Gln Leu Ala Phe Trp Pro Leu Arg Leu Phe His Ser Leu Ala  
260 265 270

Trp Gly Ser Trp Thr Pro Gly Glu Gly Val His Trp Tyr Pro Gln Leu

Untitled

275

280

285

Leu Tyr Arg Leu Gly Arg Leu Leu Leu Glu Glu Gly Ser Phe His Pro  
290 295 300

Leu Gly Met Ser Gly Ala Gly Ser  
305 310

<210> 15  
<211> 64  
<212> PRT  
<213> Danio rerio

<400> 15

Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn  
1 5 10 15

His Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp  
20 25 30

Gly His His Phe Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp  
35 40 45

Ile Thr Thr Ser Asp Arg Asp Lys Ser Lys Tyr Gly Thr Leu Ser Arg  
50 55 60

<210> 16  
<211> 64  
<212> PRT  
<213> Danio rerio

<400> 16

Gln Arg Cys Lys Glu Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn  
1 5 10 15

Met Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp  
20 25 30

Gly Asn His Phe Glu Asp Ser Leu His Tyr Glu Gly Arg Ala Val Asp

Untitled

35

40

45

Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Met Phe Ala Arg  
50 55 60

<210> 17  
<211> 64  
<212> PRT  
<213> Danio rerio

<220>  
<221> MISC\_FEATURE  
<222> (1)..(221)  
<223> Xaa=unknown amino acid

<400> 17

Gln Arg Cys Lys Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn  
1 5 10 15

Leu Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp  
20 25 30

Gly Leu His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp  
35 40 45

Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr Arg Met Leu Ala Arg  
50 55 60

<210> 18  
<211> 38  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Degenerate oligonucleotide  
<220>

<220>  
<221> misc\_feature  
<222> (1)..(36)

<223> n=inosine

Untitled

<400> 18  
ggaattccca gcagntgcta aaggaagcaa gngctnaa  
38

<210> 19  
<211> 33  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Degenerate oligonucleotide

<220>  
<221> misc\_feature  
<222> (1)..(33)  
<223> n=inosine

<400> 19  
tcatcgatgg acccagatcg aaanccngct ctc  
33

<210> 20  
<211> 29  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Degenerate oligonucleotide

<220>  
<221> misc\_feature  
<222> (1)..(27)  
<223> n=inosine

<400> 20  
gctctagagc tcnacngcna gancgtngc  
29

<210> 21  
<211> 50  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Annealed oligonucleotide lacI

<400> 21

Untitled

agctgtcgac gcggccgcta cgtaggttac cgacgtcaag cttagatctc  
50

<210> 22  
<211> 50  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Annealed oligonucleotide lac2

<400> 22  
agctgagatc taagcttgac gtcggtaacc tacgtagcgg ccgcgtcgac  
50

<210> 23  
<211> 45  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Sf-1 oligonucleotide

<400> 23  
gatcggccag gcaggcctcg cgatatcgtc accgcggtat tcgaa  
45

<210> 24  
<211> 30  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Sf-2 oligonucleotide

<400> 24  
agtgccagtc ggggccccca gggccgcgcc  
30

<210> 25  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>

<223> Oligonucleotide 137

Untitled

<400> 25  
taccacagcg gatggttcgg  
20

<210> 26  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Oligonucleotide 138

<400> 26  
gtggtggtta tgccgatcgc  
20

<210> 27  
<211> 21  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Oligonucleotide WPR2

<400> 27  
taagaggcct ataagaggcg g  
21

<210> 28  
<211> 20  
<212> DNA  
<213> Artificial Sequence

<220>  
<223> Oligonucleotide 924

<400> 28  
aagtcagccc agaggagact  
20

<210> 29  
<211> 6  
<212> PRT  
<213> Mus musculus

<400> 29

Cys Gly Pro Gly Arg Gly

1

5

<210> 30  
 <211> 29  
 <212> DNA  
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<220>  
 <223> Degenerate oligonucleotide hh5.1

<220>  
 <221> misc\_feature  
 <222> (1)..(29)  
 <223> n=inosine

<400> 30  
 agcagntgct aaaggaagca agngctnaa  
 29

<210> 31  
 <211> 23  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Degenerate oligonucleotide hh3.3

<220>  
 <221> misc\_feature  
 <222> (1)..(23)  
 <223> n=inosine

<400> 31  
 ctcnacngcn aganckgtng cna  
 23

<210> 32  
 <211> 32  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Oligonucleotide to amplify Shh ORF

<400> 32  
 ctgcagggat ccaccatgcg gcttttgacg ag  
 32



# Untitled

<210> 33  
 <211> 31  
 <212> DNA  
 <213> Artificial Sequence

<220>  
 <223> Oligonucleotide to amplify Shh ORF

<400> 33  
 ctgcagggat ccttattcca cacgagggat t  
 31

<210> 34  
 <211> 471  
 <212> PRT  
 <213> Drosophila melanogaster

<400> 34

Met Asp Asn His Ser Ser Val Pro Trp Ala Ser Ala Ala Ser Val Thr  
 1 5 10 15

Cys Leu Ser Leu Gly Cys Gln Met Pro Gln Phe Gln Phe Gln Phe Gln  
 20 25 30

Leu Gln Ile Arg Ser Glu Leu His Leu Arg Lys Pro Ala Arg Arg Thr  
 35 40 45

Gln Thr Met Arg His Ile Ala His Thr Gln Arg Cys Leu Ser Arg Leu  
 50 55 60

Thr Ser Leu Val Ala Leu Leu Leu Ile Val Leu Pro Met Val Phe Ser  
 65 70 75 80

Pro Ala His Ser Cys Gly Pro Gly Arg Gly Leu Gly Arg His Arg Ala  
 85 90 95

Arg Asn Leu Tyr Pro Leu Val Leu Lys Gln Thr Ile Pro Asn Leu Ser  
 100 105 110

Glu Tyr Thr Asn Ser Ala Ser Gly Pro Leu Glu Gly Val Ile Arg Arg

Untitled

115

120

125

Asp Ser Pro Lys Phe Lys Asp Leu Val Pro Asn Tyr Asn Arg Asp Ile  
130 135 140

Leu Phe Arg Asp Glu Glu Gly Thr Gly Ala Asp Gly Leu Met Ser Lys  
145 150 155 160

Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn Glu  
165 170 175

Trp Pro Gly Ile Arg Leu Leu Val Thr Glu Ser Trp Asp Glu Asp Tyr  
180 185 190

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile  
195 200 205

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu  
210 215 220

Ala Val Glu Ala Gly Phe Asp Trp Val Ser Tyr Val Ser Arg Arg His  
225 230 235 240

Ile Tyr Cys Ser Val Lys Ser Asp Ser Ser Ile Ser Ser His Val His  
245 250 255

Gly Cys Phe Thr Pro Glu Ser Thr Ala Leu Leu Glu Ser Gly Val Arg  
260 265 270

Lys Pro Leu Gly Glu Leu Ser Ile Gly Asp Arg Val Leu Ser Met Thr  
275 280 285

Ala Asn Gly Gln Ala Val Tyr Ser Glu Val Ile Leu Phe Met Asp Arg  
290 295 300

Asn Leu Glu Gln Met Gln Asn Phe Val Gln Leu His Thr Asp Gly Gly

Untitled

305 310 315 320

Ala Val Leu Thr Val Thr Pro Ala His Leu Val Ser Val Trp Gln Pro  
325 330 335

Glu Ser Gln Lys Leu Thr Phe Val Phe Ala His Arg Ile Glu Glu Lys  
340 345 350

Asn Gln Val Leu Val Arg Asp Val Glu Thr Gly Glu Leu Arg Pro Gln  
355 360 365

Arg Val Val Lys Leu Gly Ser Val Arg Ser Lys Gly Val Val Ala Pro  
370 375 380

Leu Thr Arg Glu Gly Thr Ile Val Val Asn Ser Val Ala Ala Ser Cys  
385 390 395 400

Tyr Ala Val Ile Asn Ser Gln Ser Leu Ala His Trp Gly Leu Ala Pro  
405 410 415

Met Arg Leu Leu Ser Thr Leu Glu Ala Trp Leu Pro Ala Lys Glu Gln  
420 425 430

Leu His Ser Ser Pro Lys Val Val Ser Ser Ala Gln Gln Gln Asn Gly  
435 440 445

Ile His Trp Tyr Ala Asn Ala Leu Tyr Lys Val Lys Asp Tyr Val Leu  
450 455 460

Pro Gln Ser Trp Arg His Asp  
465 470

<210> 35  
<211> 73  
<212> PRT  
<213> Gallus gallus

<400> 35

# Untitled

Arg Cys Lys Glu Arg Val Asn Ser Leu Ala Ile Ala Val Met His Met  
1 5 10 15

Trp Pro Gly Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly  
20 25 30

His His Leu Pro Asp Ser Leu His Tyr Glu Gly Arg Ala Leu Asp Ile  
35 40 45

Thr Thr Ser Asp Arg Asp Arg His Lys Tyr Gly Met Leu Ala Arg Leu  
50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val  
65 70

<210> 36

<211> 73

<212> PRT

<213> Gallus gallus

<400> 36

Arg Cys Lys Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln  
1 5 10 15

Trp Pro Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly  
20 25 30

His His Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile  
35 40 45

Thr Thr Ser Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu  
50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val  
65 70

<210> 37

<211> 64

# Untitled

<212> PRT

<213> Danio rerio

<400> 37

Lys Arg Cys Lys Glu Lys Leu Asn Val Leu Ala Tyr Ser Val Met Asn  
1 5 10 15

Glu Trp Pro Gly Ile Arg Leu Val Val Thr Glu Ser Trp Asp Glu Asp  
20 25 30

Tyr His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr  
35 40 45

Ile Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg  
50 55 60

<210> 38

<211> 28

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate primer

<220>

<221> misc\_feature

<222> (1)..(28)

<223> n=inosine

<400> 38

aaaagcttta ytgytaygtn ggnathgg  
28

<210> 39

<211> 28

<212> DNA

<213> Artificial Sequence

<220>

<223> Degenerate primer

<220>

<221> misc\_feature

<222> (1)..(28)

Untitled

<223> n=inosine

<400> 39  
aagaattcta ngcrttrtar ttrttngg  
28

<210> 40  
<211> 221  
<212> PRT  
<213> Artificial Sequence

<220>  
<223> Description of Artificial Sequence: Degenerate Shh  
polypeptide general formula

<220>  
<221> SITE  
<222> (7)  
<223> Xaa=Gly, Ala, Val, Leu, Ile, Phe, Tyr, or Trp

<220>  
<221> SITE  
<222> (9)  
<223> Xaa=Arg, His or Lys

<220>  
<221> SITE  
<222> (44)  
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser. or Thr

<220>  
<221> SITE  
<222> (85)  
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<220>  
<221> SITE  
<222> (93)  
<223> Xaa=Lys, Arg, His, Asn, or Gln

<220>  
<221> SITE  
<222> (98)  
<223> Xaa=Lys, Arg or His

<220>  
<221> SITE

Untitled

<222> (112)  
<223> Xaa=Ser, Thr, Tyr, Trp, or Phe

<220>  
<221> SITE  
<222> (132)  
<223> Xaa=Lys, Arg or His

<220>  
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<222> (137)  
<223> Xaa=Met, Cys, Ser, or Thr

<220>  
<221> SITE  
<222> (139)  
<223> Xaa=Gly, Ala, Val, Leu, Ile, Ser, or Thr

<220>  
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<222> (181)  
<223> Xaa=Leu, Val, Met, Thr, or Ser

<220>  
<221> SITE  
<222> (183)  
<223> Xaa=His, Phe, Tyr, Ser, Thr, Met, or Cys

<220>  
<221> SITE  
<222> (185)  
<223> Xaa=Gln, Asn, Glu, or Asp

<220>  
<221> SITE  
<222> (186)  
<223> Xaa=His, Phe, Tyr, Thr, Gln, Asn, Glu, or Asp

<220>  
<221> SITE  
<222> (189)  
<223> Xaa=Gln, Asn, Glu, Asp, Thr, Ser, Met, or Cys

<220>  
<221> SITE  
<222> (191)  
<223> Xaa=Ala, Gly, Cys, Leu, Val, or Met

Untitled

<220>  
<221> SITE  
<222> (196)  
<223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, Glu, Gln, Ser,  
Thr, or Cys

<220>  
<221> SITE  
<222> (200)  
<223> Xaa=Arg, Lys, Met, or Ile

<220>  
<221> SITE  
<222> (206)  
<223> Xaa=Ala, Gly, Cys, Asp, Glu, Gln, Asn, Ser, Thr,  
or Met

<220>  
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<222> (207)  
<223> Xaa=Ala, Gly, Cys, Asp, Asn, Glu, or Gln

<220>  
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<222> (209)  
<223> Xaa=Arg, Lys, Met, Ile, Asn, Asp, or Glu

<220>  
<221> SITE  
<222> (211)  
<223> Xaa=Leu, Val, Met, or Ile

<220>  
<221> SITE  
<222> (212)  
<223> Xaa=Phe, Tyr, Thr, His, or Trp

<220>  
<221> SITE  
<222> (216)  
<223> Xaa=Ile, Val, Leu, or Met

<220>  
<221> SITE  
<222> (217)  
<223> Xaa=Met, Cys, Ile, Leu, Val, Thr, or Ser

<220>



# Untitled

<221> SITE

<222> (219)

<223> Xaa=Leu, Val, Met, Thr, or Ser

<400> 40

Cys Gly Pro Gly Arg Gly Xaa Gly Xaa Arg Arg His Pro Lys Lys Leu  
1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr  
20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Xaa Arg Asn Ser Glu  
35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys  
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys  
65 70 75 80

Asp Lys Leu Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp Pro Gly  
85 90 95

Val Xaa Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Xaa  
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser  
115 120 125

Asp Arg Asp Xaa Ser Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala Val Glu  
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys  
145 150 155 160

Ser Val Lys Ala Glu Asn Ser Val Ala Ala Lys Ser Gly Gly Cys Phe  
165 170 175

Pro Gly Ser Ala Xaa Val Xaa Leu Xaa Xaa Gly Gly Xaa Lys Xaa Val  
180 185 190

Lys Asp Leu Xaa Pro Gly Asp Xaa Val Leu Ala Ala Asp Xaa Xaa Gly  
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210 215 220

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<211> 167  
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<213> Artificial Sequence

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hedgehog polypeptide general formula

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<223> Xaa=Gly, Ala, Val, Leu, or Ile

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<223> Xaa=Gly, Ala, Val, Leu, Ile, Lys, His, or Arg

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<222> (12)  
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<222> (13)  
<223> Xaa=Phe, Trp or Tyr or an amino acid gap

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gap

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<220>

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<220>

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			20					25					30		

# Untitled

Xaa Thr Leu Gly Ala Ser Gly Xaa Xaa Glu Gly Xaa Xaa Xaa Arg Xaa  
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 Ser Glu Arg Phe Xaa Xaa Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile  
 50 55 60  
 Phe Lys Asp Glu Glu Asn Xaa Gly Ala Asp Arg Leu Met Thr Xaa Arg  
 65 70 75 80  
 Cys Lys Xaa Xaa Xaa Asn Xaa Leu Ala Ile Ser Val Met Asn Xaa Trp  
 85 90 95  
 Pro Gly Val Xaa Leu Arg Val Thr Glu Gly Xaa Asp Glu Asp Gly His  
 100 105 110  
 His Xaa Xaa Xaa Ser Leu His Tyr Glu Gly Arg Ala Xaa Asp Ile Thr  
 115 120 125  
 Thr Ser Asp Arg Asp Xaa Xaa Lys Tyr Gly Xaa Leu Xaa Arg Leu Ala  
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 His Xaa Ser Val Lys Xaa Xaa  
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tcccacctcg aaaccctcgg cagctccgtg caaaagcacg cgggcaaggt gctattcgtg 2  
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# Untitled

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cagaccaagc tgattctcaa gaaagtggga ccgagcatcc tgttcagtgc ctgcagcacc 16  
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# Untitled

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gccattccgg cagtcatact catcctcagc gtgggcatga tgctgtgctt caatgtgctg 20	31
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60

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cccgtgcgca gcagcaagag atcgggcaaa tcctatgtgg tgcagggatc gcgatcctcg 34  
80

cgaggcagct gccagaagtc gcatcaccac caccacaaag accttaatga tccatcgctg 35  
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gtgacggtgg agacgacgca ctcgacagc aacaccacca aggtgacggc cacggccaac 38  
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20 25 30

His His Gly Gln Glu Ser Leu His Tyr Glu Gly Arg Ala Val Thr Ile  
35 40 45

Ala Thr Ser Asp Arg Asp Gln Ser Lys Tyr Gly Met Leu Ala Arg Leu  
50 55 60

Ala Val Glu Ala Gly Phe Asp Trp Val  
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<210> 48  
<211> 167  
<212> PRT  
<213> Mus musculus

<400> 48

Cys Gly Pro Gly Arg Gly Pro Val Gly Arg Arg Arg Tyr Val Arg Lys  
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Gln Leu Val Pro Leu Leu Tyr Lys Gln Phe Val Pro Ser Met Pro Glu  
20 25 30

Arg Thr Leu Gly Ala Ser Gly Pro Ala Glu Gly Arg Val Thr Arg Gly  
35 40 45

Ser Glu Arg Phe Arg Asp Leu Val Pro Asn Tyr Asn Pro Asp Ile Ile  
50 55 60

Phe Lys Asp Glu Glu Asn Ser Gly Ala Asp Arg Leu Met Thr Glu Arg  
65 70 75 80

Cys Lys Glu Arg Val Asn Ala Leu Ala Ile Ala Val Met Asn Met Trp  
85 90 95

Pro Gly Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His  
100 105 110

# Untitled

His Ala Gln Asp Ser Leu His Tyr Glu Gly Arg Ala Leu Asp Ile Thr  
115 120 125

Thr Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala  
130 135 140

Val Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Arg Asn His Ile  
145 150 155 160

His Val Ser Val Lys Ala Asp  
165

<210> 49  
<211> 118  
<212> PRT  
<213> Mus musculus

<400> 49

Glu Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe  
1 5 10 15

Lys Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys  
20 25 30

Lys Asp Arg Leu Asn Ser Leu Ala Ile Ser Val Met Asn Gln Trp Pro  
35 40 45

Gly Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His  
50 55 60

Ser Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr  
65 70 75 80

Ser Asp Arg Asp Arg Asn Lys Tyr Gly Leu Leu Ala Arg Leu Ala Val  
85 90 95

Untitled

Glu Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Val His  
 100 105 110

Cys Ser Val Lys Ser Glu  
 115

<210> 50  
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 <212> PRT  
 <213> Homo sapiens

<400> 50

Arg Arg Leu Met Thr Gln Arg Cys Lys Asp Arg Leu Asn Ser Leu Ala  
 1 5 10 15

Ile Ser Val Met Asn Gln Trp Pro Gly Val Lys Leu Arg Val Thr Glu  
 20 25 30

Gly Trp Asp Glu Asp Gly His His Ser Glu Glu Ser Leu His Tyr Glu  
 35 40 45

Gly Arg Ala Val Asp Ile Thr Thr Ser Asp Arg Asp Arg Asn Lys Tyr  
 50 55 60

Gly Leu Leu Ala Arg Leu Ala Val Glu Ala Gly Phe Asp Trp Val Tyr  
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Tyr Glu Ser Lys Ala His Val His Cys Ser Val Lys Ser Glu  
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<210> 51  
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 <212> PRT  
 <213> Homo sapiens

<400> 51

Cys Gly Pro Gly Arg Gly Phe Gly Lys Arg Arg His Pro Lys Lys Leu  
 1 5 10 15

Untitled

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr  
20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Ser Arg Asn Ser Glu  
35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys  
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys  
65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly  
85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser  
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser  
115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu  
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys  
145 150 155 160

Ser Val Lys Ala Glu  
165

<210> 52  
<211> 165  
<212> PRT  
<213> Gallus gallus

<400> 52

Cys Gly Pro Gly Arg Gly Ile Gly Lys Arg Arg His Pro Lys Lys Leu  
1 5 10 15



# Untitled

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr  
20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu  
35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys  
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys  
65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly  
85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser  
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser  
115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu  
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys  
145 150 155 160

Ser Val Lys Ala Glu  
165

<210> 53  
<211> 165  
<212> PRT  
<213> Mus musculus

<400> 53

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20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu  
35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys  
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys  
65 70 75 80

Asp Lys Leu Asn Ala Leu Ala Ile Ser Val Met Asn Gln Trp Pro Gly  
85 90 95

Val Arg Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Ser  
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser  
115 120 125

Asp Arg Asp Arg Ser Lys Tyr Gly Met Leu Ala Arg Leu Ala Val Glu  
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys  
145 150 155 160

Ser Val Lys Ala Glu  
165

<210> 54

<211> 165

<212> PRT

<213> Danio rerio

# Untitled

<400> 54

Cys Gly Pro Gly Arg Gly Tyr Gly Arg Arg Arg His Pro Lys Lys Leu  
1 5 10 15

Thr Pro Leu Ala Tyr Lys Gln Phe Ile Pro Asn Val Ala Glu Lys Thr  
20 25 30

Leu Gly Ala Ser Gly Arg Tyr Glu Gly Lys Ile Thr Arg Asn Ser Glu  
35 40 45

Arg Phe Lys Glu Leu Thr Pro Asn Tyr Asn Pro Asp Ile Ile Phe Lys  
50 55 60

Asp Glu Glu Asn Thr Gly Ala Asp Arg Leu Met Thr Gln Arg Cys Lys  
65 70 75 80

Asp Lys Leu Asn Ser Leu Ala Ile Ser Val Met Asn His Trp Pro Gly  
85 90 95

Val Lys Leu Arg Val Thr Glu Gly Trp Asp Glu Asp Gly His His Phe  
100 105 110

Glu Glu Ser Leu His Tyr Glu Gly Arg Ala Val Asp Ile Thr Thr Ser  
115 120 125

Asp Arg Asp Lys Ser Lys Tyr Gly Thr Leu Ser Arg Leu Ala Val Glu  
130 135 140

Ala Gly Phe Asp Trp Val Tyr Tyr Glu Ser Lys Ala His Ile His Cys  
145 150 155 160

Ser Val Lys Ala Glu  
165

<210> 55

<211> 18

Untitled

<212> PRT

<213> Artificial Sequence

<220>

<223> N-terminal exogenous leader

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Met	Gly	Ser	Ser	His	His	His	His	His	His	Leu	Val	Pro	Arg	Gly	Ser
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